

Amendments to the Specification:

On page 60, replace paragraph 31, lines 15-20, with the following:

[31] In another preferred embodiment, the present invention provides a novel method of treating rheumatoid arthritis in a patient comprising: administering a therapeutic radiopharmaceutical ~~of Embodiment 19~~ according to one embodiment capable of localizing in new angiogenic vasculature to a patient by injection or infusion.

On page 60, replace paragraph 32, lines 22-26, with the following:

[32] In another preferred embodiment, the present invention provides a novel method of treating cancer in a patient comprising: administering to a patient in need thereof a therapeutic radiopharmaceutical ~~of Embodiment 19~~ according to one embodiment by injection or infusion.

On page 60, replace paragraph 33, lines 28-32, continuing to page 61, same paragraph, lines 1-2 with the following:

[33] In another preferred embodiment, the present invention provides a novel method of treating restenosis in a patient comprising: administering to a patient, either systemically or locally, a therapeutic radiopharmaceutical ~~of Embodiment 19~~ according to one embodiment capable of localizing in the restenotic area and delivering an effective dose of radiation.

On page 61, replace paragraph 34, lines 4-11, with the following:

[34] In another preferred embodiment, the present invention provides a novel method of imaging therapeutic angiogenesis in a patient comprising: (1) administering a diagnostic radiopharmaceutical, a MRI contrast agent, or a X-ray contrast agent ~~of Embodiment 11~~ according to one embodiment to a patient by

injection or infusion; (2) imaging the area of the patient wherein the desired formation of new blood vessels is located.

On page 61, replace paragraph 35, lines 13-20, with the following:

[35] In another preferred embodiment, the present invention provides a novel method of imaging atherosclerosis in a patient comprising: (1) administering a diagnostic radiopharmaceutical, a MRI contrast agent, or a X-ray contrast agent ~~of Embodiment 11~~ according to one embodiment to a patient by injection or infusion; (2) imaging the area of the patient wherein the atherosclerosis is located.

On page 61, replace paragraph 36, lines 22-28, with the following:

[36] In another preferred embodiment, the present invention provides a novel method of imaging restenosis in a patient comprising: (1) administering a diagnostic radiopharmaceutical, a MRI contrast agent, or a X-ray contrast agent ~~of Embodiment 11~~ according to one embodiment to a patient by injection or infusion; (2) imaging the area of the patient wherein the restenosis is located.

On page 61, replace paragraph 37, lines 30-36, with the following:

[37] In another preferred embodiment, the present invention provides a novel method of imaging cardiac ischemia in a patient comprising: (1) administering a diagnostic radiopharmaceutical, a MRI contrast agent, or a X-ray contrast agent ~~of Embodiment 11~~ according to one embodiment to a patient by injection or infusion; (2) imaging the area of the myocardium wherein the ischemic region is located.

On page 62, replace paragraph 38, lines 1-8, with the following:

[38] In another preferred embodiment, the present invention provides a novel method of imaging myocardial reperfusion injury in

a patient comprising: (1) administering a diagnostic radiopharmaceutical, a MRI contrast agent, or a X-ray contrast agent of ~~Embodiment 11~~ according to one embodiment to a patient by injection or infusion; (2) imaging the area of myocardium wherein the reperfusion injury is located.

On page 62, replace paragraph 39, lines 10-16, with the following:

[39] In another preferred embodiment, the present invention provides a novel method of imaging cancer in a patient comprising: (1) administering a diagnostic radiopharmaceutical of ~~Embodiment 12~~ according to one embodiment to a patient by injection or infusion; (2) imaging the patient using planar or SPECT gamma scintigraphy, or positron emission tomography.

On page 62, replace paragraph 40, lines 18-22, with the following:

[40] In another preferred embodiment, the present invention provides a novel method of imaging cancer in a patient comprising: (1) administering a MRI contrast agent of ~~Embodiment 27~~ according to one embodiment; and (2) imaging the patient using magnetic resonance imaging.

On page 62, replace paragraph 41, lines 24-28, with the following:

[41] In another preferred embodiment, the present invention provides a novel method of imaging cancer in a patient comprising: (1) administering a X-ray contrast agent of ~~Embodiment 30~~ according to one embodiment; and (2) imaging the patient using X-ray computed tomography.

On page 82, replace paragraph 47, lines 9-17, with the following:

[47] In another more preferred embodiment, the present invention provides a novel ultrasound contrast agent composition, comprising:  
(a) a compound of ~~Embodiment 44~~ according to one embodiment, comprising: an indazole that binds to the integrin  $\alpha_v\beta_3$  or  $\alpha_v\beta_5$  a

surfactant and a linking group between the indazole and the surfactant;

- (b) a parenterally acceptable carrier; and,
- (c) an echogenic gas.

On page 82, replace paragraph 50, lines 30-35, with the following:

[50] In another preferred embodiment, the present invention provides a method of imaging cancer in a patient comprising: (1) administering, by injection or infusion, a ultrasound contrast agent composition of ~~Embodiment 44~~ according to one embodiment to a patient; and (2) imaging the patient using sonography.

On page 83, replace paragraph 51, lines 1-8, with the following:

[51] In another preferred embodiment, the present invention provides a method of imaging therapeutic angiogenesis in a patient comprising: (1) administering, by injection or infusion, an ultrasound contrast agent composition of ~~Embodiment 42~~ according to one embodiment to a patient; (2) imaging the area of the patient wherein the desired formation of new blood vessels is located.

On page 83, replace paragraph 52, lines 10-15, with the following:

[52] In another preferred embodiment, the present invention provides a method of imaging atherosclerosis in a patient comprising: (1) administering, by injection or infusion, an ultrasound contrast agent composition of ~~Embodiment 42~~ according to one embodiment to a patient; (2) imaging the area of the patient wherein the atherosclerosis is located.

On page 83, replace paragraph 53, lines 17-22, with the following:

[53] In another preferred embodiment, the present invention provides a method of imaging restenosis in a patient comprising: (1) administering, by injection or infusion, an ultrasound contrast agent composition of ~~Embodiment 42~~ according to one embodiment to a

patient; (2) imaging the area of the patient wherein the restenosis is located.

On page 83, replace paragraph 54, lines 24-29, with the following:

[54] In another preferred embodiment, the present invention provides a method of imaging cardiac ischemia in a patient comprising: (1) administering, by injection or infusion, an ultrasound contrast agent composition of ~~Embodiment 42~~ according to one embodiment to a patient; (2) imaging the area of the myocardium wherein the ischemic region is located.

On page 83, replace paragraph 55, lines 31-37, with the following:

[55] In another preferred embodiment, the present invention provides a method of imaging myocardial reperfusion injury in a patient comprising: (1) administering, by injection or infusion, an ultrasound contrast agent composition of ~~Embodiment 42~~ according to one embodiment to a patient; (2) imaging the area of myocardium wherein the reperfusion injury is located.

On page 84, replace paragraph 56, lines 1-7, with the following:

[56] In another preferred embodiment, the present invention provides a novel therapeutic radiopharmaceutical composition, comprising:

- (a) a therapeutic radiopharmaceutical of ~~Embodiment 19~~ according to one embodiment; and,
- (b) a parenterally acceptable carrier.

On page 84, replace paragraph 57, lines 9-21, with the following:

[57] In another preferred embodiment, the present invention provides a novel diagnostic pharmaceutical composition, comprising:

- (a) a diagnostic radiopharmaceutical, a MRI contrast agent, or a X-ray contrast agent of ~~Embodiment 11~~ according to one embodiment; and,

(b) a parenterally acceptable carrier.

On page 84, replace paragraph 58, lines 15-21, with the following:

[58] In another preferred embodiment, the present invention provides a kit for treating cancer, comprising a compound of ~~Embodiment 1~~ according to one embodiment, or a pharmaceutically acceptable salt thereof, and at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

On page 84, replace paragraph 59, lines 23-33, with the following:

[59] In another preferred embodiment, the present invention provides a kit according to ~~Embodiment 58~~ one embodiment wherein said kit comprises a plurality of separate containers, wherein at least one of said containers contains a compound of ~~Embodiment 1~~ according to another embodiment, or a pharmaceutically acceptable salt thereof, and at least another of said containers contains one or more agents selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

On page 84, replace paragraph 60, lines 35-37, continuing to page 61, same paragraph, lines 1-20, with the following:

[60] In another preferred embodiment, the present invention provides a kit according to ~~Embodiment 58~~ one embodiment, wherein the chemotherapeutic agent is selected from the group consisting of mitomycin, tretinoin, ribomustin, gemcitabine, vincristine, etoposide, cladribine, mitobronitol, methotrexate, doxorubicin, carboquone, pentostatin, nitracrine, zinostatin, cetorelix, letrozole, raltitrexed, daunorubicin, fadrozole, fotemustine, thymalfasin, sobuzoxane, nedaplatin, cytarabine, bicalutamide, vinorelbine, vesnarinone, aminoglutethimide, amsacrine, proglumide,

elliptinium acetate, ketanserine, doxifluridine, etretinate, isotretinoin, streptozocin, nimustine, vindesine, flutamide, drogenil, butocin, carmofur, razoxane, sizofilan, carboplatin, mitolactol, tegafur, ifosfamide, prednimustine, picibanil, levamisole, teniposide, improsulfan, enocitabine, lisuride, oxymetholone, tamoxifen, progesterone, mepitiostane, epitiostanol, formestane, interferon-alpha, interferon-2 alpha, interferon-beta, interferon-gamma, colony stimulating factor-1, colony stimulating factor-2, denileukin diftitox, interleukin-2, and leutinizing hormone releasing factor.

On page 85, replace paragraph 61, lines 22-38, with the following:

[61] In another preferred embodiment, the present invention provides a kit according to ~~Embodiment 58~~ one embodiment, wherein the chemotherapeutic agent is selected from the group consisting of mitomycin, tretinoin, ribomustin, gemcitabine, vincristine, etoposide, cladribine, mitobronitol, methotrexate, doxorubicin, carboquone, pentostatin, nitracrine, zinostatin, cetorelix, letrozole, raltitrexed, daunorubicin, fadrozole, fotemustine, thymalfasin, sobuzoxane, nedaplatin, cytarabine, bicalutamide, vinorelbine, vesnarinone, aminoglutethimide, amsacrine, proglumide, elliptinium acetate, ketanserine, doxifluridine, etretinate, isotretinoin, streptozocin, nimustine, vindesine, flutamide, drogenil, butocin, carmofur, razoxane, sizofilan, carboplatin, mitolactol, tegafur, ifosfamide, prednimustine, picibanil, levamisole, teniposide, improsulfan, enocitabine, and lisuride.

On page 86, replace paragraph 62, lines 2-6, with the following:

[62] In another preferred embodiment, the present invention provides a kit according to ~~Embodiment 58~~ one embodiment wherein the chemotherapeutic agent is selected from the group consisting of oxymetholone, tamoxifen, progesterone, mepitiostane, epitiostanol, and formestane.

On page 86, replace paragraph 63, lines 8-15, with the following:

[63] In another preferred embodiment, the present invention provides a kit according to ~~Embodiment 58~~ one embodiment wherein the chemotherapeutic agent is selected from the group consisting of interferon-alpha, interferon-2 alpha, interferon-beta, interferon-gamma, colony stimulating factor-1, colony stimulating factor-2, denileukin diftitox, interleukin-2, and leutinizing hormone releasing factor.

On page 86, replace paragraph 64, lines 17-26, with the following:

[64] In another preferred embodiment, the present invention provides a kit according to ~~Embodiment 58~~ one embodiment, wherein radiosensitizer agent is selected from the group consisting of 2-(3-nitro-1,2,4-triazol-1-yl)-N-(2-methoxyethyl)acetamide, N-(3-nitro-4-quinolinyl)-4-morpholinecarboxamide, 3-amino-1,2,4-benzotriazine-1,4-dioxide, N-(2-hydroxyethyl)-2-nitroimidazole-1-acetamide, 1-(2-nitroimidazol-1-yl)-3-(1-piperidinyl)-2-propanol, and 1-(2-nitro-1-imidazolyl)-3-(1-aziridino)-2-propanol.

On page 86, replace paragraph 65, lines 28-35, with the following:

[65] In another preferred embodiment, the present invention provides a therapeutic metallopharmaceutical composition according to ~~Embodiment 11~~ one embodiment, wherein the metallopharmaceutical is a therapeutic radiopharmaceutical, further comprising at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof.

On page 86, replace paragraph 66, lines 37-38, continuing to page 87, same paragraph, lines 1-22, with the following:

[66] In another preferred embodiment, the present invention provides a therapeutic metallopharmaceutical composition according to ~~Embodiment 65~~ one embodiment, wherein the chemotherapeutic agent is selected from the group consisting of mitomycin, tretinoin,



ribomustin, gemcitabine, vincristine, etoposide, cladribine, mitobronitol, methotrexate, doxorubicin, carboquone, pentostatin, nitracrine, zinostatin, cetorelix, letrozole, raltitrexed, daunorubicin, fadrozole, fotemustine, thymalfasin, sobuzoxane, nedaplatin, cytarabine, bicalutamide, vinorelbine, vesnarinone, aminoglutethimide, amsacrine, proglumide, elliptinium acetate, ketanserine, doxifluridine, etretinate, isotretinoin, streptozocin, nimustine, vindesine, flutamide, drogenil, butocin, carmofur, razoxane, sizofilan, carboplatin, mitolactol, tegafur, ifosfamide, prednimustine, picibanil, levamisole, teniposide, improsulfan, enocitabine, lisuride, oxymetholone, tamoxifen, progesterone, mepitiostane, epitioestanol, formestane, interferon-alpha, interferon-2 alpha, interferon-beta, interferon-gamma, colony stimulating factor-1, colony stimulating factor-2, denileukin diftitox, interleukin-2, and leutinizing hormone releasing factor.

On page 87, replace paragraph 67, lines 24-34, with the following:

[67] In another preferred embodiment, the present invention provides a therapeutic metallopharmaceutical composition according to ~~Embodiment 65~~ one embodiment, wherein radiosensitizer agent is selected from the group consisting of 2-(3-nitro-1,2,4-triazol-1-yl)-N-(2-methoxyethyl)acetamide, N-(3-nitro-4-quinolinyl)-4-morpholinecarboxamidine, 3-amino-1,2,4-benzotriazine-1,4-dioxide, N-(2-hydroxyethyl)-2-nitroimidazole-1-acetamide, 1-(2-nitroimidazol-1-yl)-3-(1-piperidinyl)-2-propanol, and 1-(2-nitro-1-imidazolyl)-3-(1-aziridino)-2-propanol.

On page 87, replace paragraph 68, lines 36-38, continuing to page 88, same paragraph, lines 1-5, with the following:

[68] In another preferred embodiment, the present invention provides a method of treating cancer in a patient comprising: administering to a patient in need thereof a therapeutic radiopharmaceutical ~~of Embodiment 19~~ according to one embodiment or a pharmaceutically acceptable salt thereof, and at least one agent selected from the group consisting of a chemotherapeutic agent and

a radiosensitizer agent, or a pharmaceutically acceptable salt thereof.

On page 88, replace paragraph 69, lines 7-10, with the following:

[69] In another preferred embodiment, the present invention provides a method of treating cancer according to ~~Embodiment 68~~ one embodiment, wherein the administration is by injection or infusion.

On page 88, replace paragraph 70, lines 12-15, with the following:

[70] In another preferred embodiment, the present invention provides a method according to ~~Embodiment 68~~ one embodiment wherein administering the therapeutic radiopharmaceutical and agent is concurrent.

On page 88, replace paragraph 71, lines 16-20, with the following:

[71] In another preferred embodiment, the present invention provides a method according to ~~Embodiment 68~~ one embodiment wherein administering the therapeutic radiopharmaceutical and agent is sequential.

On page 88, replace paragraph 72, lines 22-30, with the following:

[72] In another preferred embodiment, the present invention provides a method according to ~~Embodiment 68~~ one embodiment wherein the cancer is selected from the group consisting of carcinomas of the lung, breast, ovary, stomach, pancreas, larynx, esophagus, testes, liver, parotid, biliary tract, colon, rectum, cervix, uterus, endometrium, kidney, bladder, prostate, thyroid, squamous cell carcinomas, adenocarcinomas, small cell carcinomas, melanomas, gliomas, and neuroblastomas.

On page 88, replace paragraph 73, lines 32-38, continuing to page 89, same paragraph, lines 1-16, with the following:

[73] In another preferred embodiment, the present invention provides a method according to ~~Embodiment 68~~ one embodiment wherein the chemotherapeutic agent is selected from the group consisting of mitomycin, tretinoin, ribomustin, gemcitabine, vincristine, etoposide, cladribine, mitobronitol, methotrexate, doxorubicin, carboquone, pentostatin, nitracrine, zinostatin, cetorelix, letrozole, raltitrexed, daunorubicin, fadrozole, fotemustine, thymalfasin, sobuzoxane, nedaplatin, cytarabine, bicalutamide, vinorelbine, vesnarinone, aminoglutethimide, amsacrine, proglumide, elliptinium acetate, ketanserine, doxifluridine, etretinate, isotretinoin, streptozocin, nimustine, vindesine, flutamide, drogenil, butocin, carmofur, razoxane, sizofilan, carboplatin, mitolactol, tegafur, ifosfamide, prednimustine, picibanil, levamisole, teniposide, improsulfan, encitabine, lisuride, oxymetholone, tamoxifen, progesterone, mepitiostane, epitiostanol, formestane, interferon-alpha, interferon-2 alpha, interferon-beta, interferon-gamma, colony stimulating factor-1, colony stimulating factor-2, denileukin diftitox, interleukin-2, and leutinizing hormone releasing factor.

On page 89, replace paragraph 74, lines 18-27, with the following:

[74] In another preferred embodiment, the present invention provides a method according to ~~Embodiment 68~~ one embodiment wherein the radiosensitizer agent is selected from the group consisting of 2-(3-nitro-1,2,4-triazol-1-yl)-N-(2-methoxyethyl)acetamide, N-(3-nitro-4-quinolinyl)-4-morpholinecarboxamide, 3-amino-1,2,4-benzotriazine-1,4-dioxide, N-(2-hydroxyethyl)-2-nitroimidazole-1-acetamide, 1-(2-nitroimidazol-1-yl)-3-(1-piperidinyl)-2-propanol, and 1-(2-nitro-1-imidazolyl)-3-(1-aziridino)-2-propanol.